

REMARKS

Reconsideration and withdrawal of any rejections of the application, and allowance of the claims, especially in view of the remarks made herein, are respectfully requested.

I. STATUS OF THE CLAIMS

Claims 47-74 are pending in the application. By this paper claims 47, 55, 56, 61, 63, and 65 have been amended, claims 53, 54, 57-60, 64, and 67-72 have been canceled, and new claims 73 and 74 have been added, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel.

No new matter is added. Support the amended claims, and new claims 73 and 74, is found throughout the specification and from the originally filed claims. Specifically, support for determining the relative number of CD45 low cells in a population comprising CD45 low and CD45 high cells, as recited in amended claim 47, is found on page 20 of the specification in the section entitled "Labelled Antibodies", and on page 34 in the section entitled "CD45 and CD14 Panel". Support for determining the relative number of CD45 low cells in a population by flow cytometry, as recited in new claims 73 and 74, is found on page 20 of the specification in the sections entitled "Labelled Antibodies" and "Flow Cytometry", and on page 34 in the section entitled "CD45 and CD14 Panel".

It is respectfully submitted that the claims herewith and the claims as originally presented are and were in full compliance with the requirements of 35 U.S.C. §§101, 102, 103 and 112. The amendments and additions to these claims, and remarks concerning these claims, were not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather for clarification and to round out the scope of protection to which the Applicant is entitled.

II. OBJECTION TO AMENDMENT OF THE SPECIFICATION

In a previous Amendment, deletion of the sentence beginning on page 34, line 5, that reads "the delineation of CD45 low, CD45high, and CD45 medium is arbitrary" was requested. The present Office Action has objected to this Amendment, stating that the deletion of this sentence would constitute new matter, and change the concept of what is meant by CD45 low. Applicants respectfully disagree.

The reason for requesting this deletion, as stated previously, was that this statement was clearly made in error. Applicants maintain that this statement was clearly made in error. The designation of cells as CD45 low, medium, or high, is clearly not arbitrary – the Applicants did not intend that CD45 low cells could express high levels of CD45 antigen, and CD45 high cells could express low levels of CD45 antigen. Instead the delineation between CD45 low, medium, and high cells, is a relative or comparative one. Clearly this was the intention of the Applicants. CD45 low cells are cells having a lower level of CD45 expression than CD45 high cells, and CD45 high cells are cells having a higher level of CD45 expression than CD45 low cells. Comparative measures of antigen density are perfectly valid in the art, and in situations where fluorescence based detection methods are used, comparative measures are frequently the norm. The meaning of these terms, that is in describing cells expressing either relatively low, levels of CD45, medium levels of CD45, or relatively high levels of CD45, would have been apparent to one of skill in the art in reading the specification, especially given the common usage of these terms in the art. In this regard, the Examiner's attention is respectfully directed to the enclosed article by Sedgwick et al., which was published in 1991, well before the filing of the prior application. On page 7439 of Sedgwick et al., the authors state that “distinct populations of cells defined by staining with an anti-rat CD45 mAb were detected: (i) a high-expressing population, which was in the majority (CD45high); [and] (ii) a low expressing population (CD45low)”. This article is representative of a large number of articles that use the terms CD45high and CD45low, many of which were published before the filing of the present application.

Thus, deleting this sentence will not change the concept of what is meant by CD45 low, CD45 medium, or CD45 high. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

III. OBJECTIONS TO THE CLAIMS

Claims 57-59 are objected to as being of improper dependent form because they allegedly fail to limit the subject matter of the claim 56 on which they depend. By this paper claims 57-59 are canceled, thus rendering this objection moot. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

IV. REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The Office Action the Examiner has maintained the previous rejection of claims 47-72 alleging that because the term “CD45low” is an arbitrary term it therefore renders the claims indefinite. The Examiner asserts that the specification provides no method or standard for ascertaining the requisite degree of CD45 expression that is required for CD45 low cells, and therefore one of skill in the art would not be aware of the scope of the invention.

In response to previous rejections of this nature, we provided the Examiner with various scientific articles in which the terms “low” and “high” or the symbols “+” “+++” were used to designate antigen density, and argued that the meaning of such terms/designators was well known in the art at the time of the invention. However, the Office Action asserts that, while the use of such comparative terms may be acceptable in the scientific literature, the terms are not sufficiently definite for the purpose of patentability.

We respectfully disagree with the rejection. The terms “CD45low” and “CD45 high” are not arbitrary terms but are relative or comparative terms. The Applicant’s use of the term “arbitrary” in the specification was clearly made in error. Instead, Applicant’s clearly intended to state that the designation of cells as “CD45 low” or “CD45 high” is a relative or comparative term. Clearly Applicant’s intention was to define cells with a lower level of CD45 expression than CD45 high cells as “CD45 low”, and cells with a detectably higher level of CD45 expression, as compared to CD45 low cells, as “CD45 high” cells.

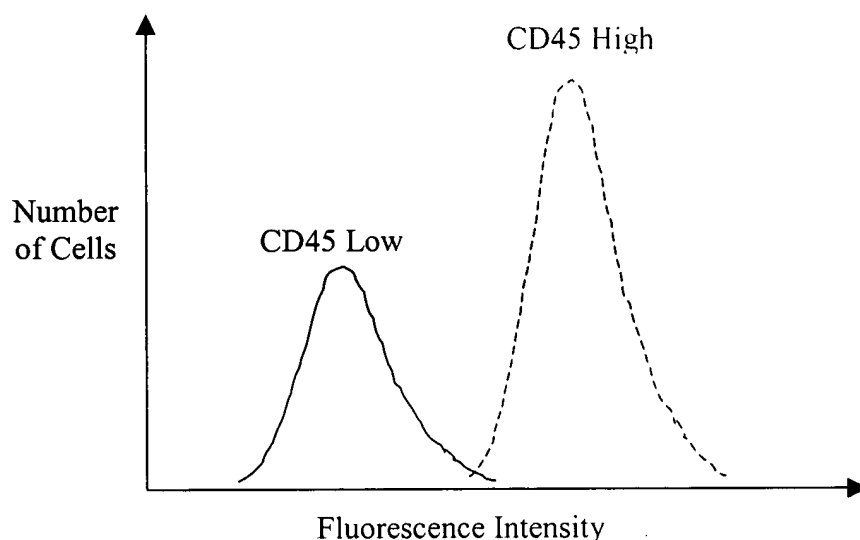
We respectfully traverse the Examiner’s assertion that even such relative terms are indefinite. By the amendment to claim 47 presented herein, we have clarified that the term “CD45 low” does have a clear meaning, and is a comparative or relative measure, not a quantitative measure. According to the present invention, and as now recited in amended claim 47, a discrete sub-population of CD45 low cells can readily be identified in a cell population that comprises at least two distinct cell populations with differing antigen density, one having a low CD45 antigen density (namely a “CD45 low” population) and the other having a high CD45 antigen density (namely a “CD45 high” population).

The methods of the invention utilize antibody-based detection (such as flow cytometry based methods) to detect levels of CD45 expression. Such antibody-based detection methods are not inherently quantitative and are most frequently used to provide relative or comparative data. These methods clearly do not measure the actual amount of CD45 protein, but rather allow a

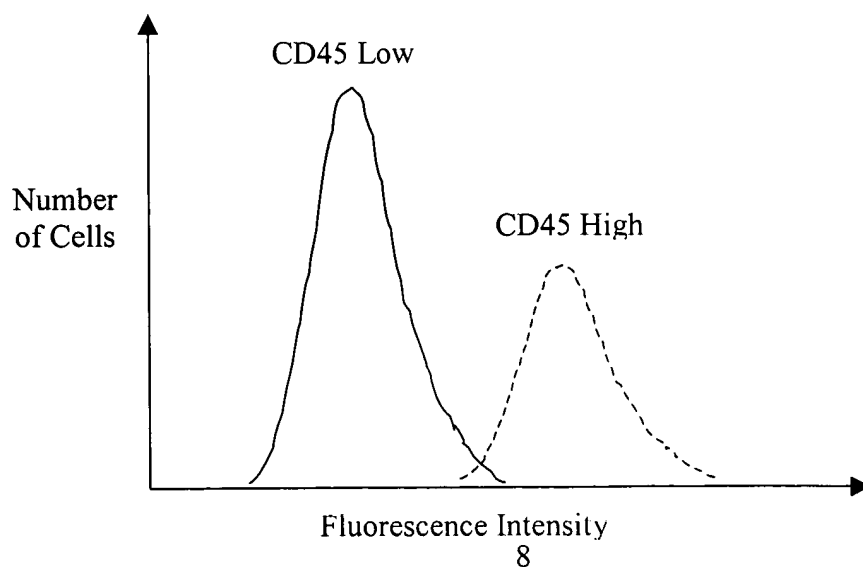
comparative measure to be made, for example based on fluorescence intensity. It is routine practice to use such relative/comparative measures when using immunological detection methods such as flow cytometry.

Below is a schematic representation illustrating the type of data that can be obtained using flow cytometry with CD45 labeled antibodies. Please note that this is not actual data, but is merely a schematic representation provided for illustrative purposes.

Before Treatment



After Treatment



Clearly, following binding of a fluorescently labeled anti-CD45 antibody to the cells of the cell population, one of skill in the art would be able to determine by flow cytometry, or indeed by other immunological detection methods, that the cell population comprises at least two sub-populations, one having a relatively low level of CD45 expression, and one having a relatively high level of CD45 expression. The Examiner appears to assert that one would not know if a given cell was a CD45 low or CD45 high cell. However, as illustrated here, and as recited in amended claim 1, one would know that one was in a possession of sub-population of CD45 high and/or CD45 low cells in the context of the cell population as a whole. Similarly, one would readily be able to determine whether a shift in the relative number of CD45 low and CD45 high cells occurred using such methods.

Further evidence that one of skill in the art would know how to identify and sub-population of CD45 high and/or CD45 low cells in the context of a cell population as a whole, and would readily be able to detect a shift in the relative number of CD45 low and CD45 high cells, is provided by Sedgwick et al. which was published in 1991, well before the filing of the present application. The Examiner's attention is directed to Figure 1 of Sedgwick et al. which provides flow cytometry data clearly illustrating the presence of a CD45 high, a CD45 low, and a CD45 negative sub-population of cells, and illustrating a shift in the relative number of cells in each sub-population following infection of cells with a coronavirus.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

V. REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The present Office Action makes several rejections of the claims under the first paragraph of section §112, as follows:

The Office Action alleges that, since there is no teaching in the application that CD45low cells express MHC class I or II antigens, claim 53 contains new subject matter not present in the application as filed and is therefore fails to comply with the written description requirement of section 35 U.S.C. §112 (first paragraph). By this paper claim 53 is canceled, thereby overcoming this rejection.

The Office Action alleges that claims 67-72 contain new subject matter not present in the application as filed because the application fails to teach or demonstrate that CD45low cells have

the properties of the recited in these claims. By this paper claims 67-72 are cancelled, thereby overcoming this rejection.

The Office Action alleges that claims 47-72 contain subject matter that was not described in the specification in such as way as to reasonably convey to one of skill in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action asserts that the Applicant was not in possession of the genus of “agents” that operably engage the committed cells. However, the Office Action does concede that the specification is enabling for antibodies to the beta chain of MHC class I and II receptors. By the amendments to the claims presented herein, this rejection is overcome.

The Office Action alleges that claims 63-65 contain subject matter which was not described in the specification in such as way as to reasonably convey to one of skill in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts that the Applicant was not in possession of the genus of “biological response modifiers” to be used in conjunction with the “agents” of claim 47, but admits that the specification is enabling for biological response modifiers that are alkylating agents. By the amendment to claims 63-65 presented herein, this rejection is overcome.

The Office Action alleges that claims 47-61 and 63-72 are only enabling for agents which are antibodies directed to the alpha or beta chains of MHC class I or II receptors, and not for the entire genus of “agents”. The amendment to claim 47 presented herein overcomes this rejection.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

VI. REJECTIONS UNDER 35 U.S.C. §101/112, FIRST PARAGRAPH

The Office Action maintains the previous combined rejection of the claims under sections §101 and §112, alleging that the claimed invention (claims 47-76) is not supported by either an asserted utility or a well established utility as required by 35 U.S.C. §101, and that as such, one of skill in the art would not know how to make and use the claimed invention, as required by 35 U.S.C. §112. Specifically, the Examiner asserts that the specification fails to mention any use for CD45low cells.

The CD45 low cell population is described in the specification on pages 28-29, page 34, in Table 6, Table 8, and in Charts 1-5.

The Examiner is respectfully reminded that the specification must be read in the context of the state of the art at the time of filing. It is respectfully submitted that, at the time of filing, an individual of skill in the art would have been readily aware of the usefulness of undifferentiated cells possessing CD45 low markers. This very sentiment was presented by the Applicant in the Declaration filed on September 6, 2002. The Examiner's attention is respectfully drawn to section 5 this declaration, entitled "Utility." The text of the section is set forth below:

As would have been readily understood at the priority date of the present invention, i.e. at February 2, 1995, CD45low is a marker found on stem cells having a haemopoietic or myeloid nature. A skilled person at the priority date of the above-identified application would have readily understood that undifferentiated cells with CD45low markers could be used in the production of, *inter alia*, more committed haematopoietic cells, for example white blood cells. Thus, CD45low cells could be redjfferentiated into more committed haematopoietic cells for instance, and thus a skilled person would have readily understood that the CD45low cells had a utility in the treatment of, for example, leukaemia.

Thus, one of skill in the art would recognize the value of being able to, *inter alia*, increase the relative number of CD45 low cells in a cell population. Furthermore, the teaching in the specification, as found on pages 28-29 and 34, would provide one of skill in the art with the methods of accomplishing the same.

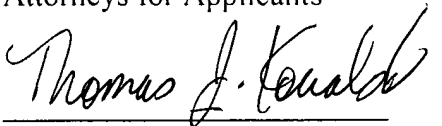
Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

In light of the amendments and remarks made herein, it is respectfully submitted that the application is now in condition for allowance. Early and favorable reconsideration of the application, reconsideration and withdrawal of the rejections of the application, and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

By: 

Thomas J. Kowalski
Reg. No. 32,147
Tel (212) 588-0800
Fax (212) 588-0500
Email TKowalski@FLHLaw.com